REMARKS

Applicant traverses the rejections of claims 1-3, 5-9, 11-14, 27-31, 34, 36 and 37 as being unpatentable under 35 U.S.C. 103(a) over Boyce et al. 5,899,939 and claims 4, 10, 15-26, 32, 33 and 35 as being unpatentable by combining Boyce et al. '939 with Boyce et al. 6,294,187. The rejection of the claims under 35 U.S.C. 112 is also traversed.

The present invention is a bone sheet taken from a tubular bone using both the cortical and cancellous portions of the tubular bone. The portions are demineralized, leaving a single integral sheet having residual calcium content of a specified range for surgical usage. Previously, it had been believed that the cancellous portion could not be used in a structural device and bone sheets were taken from cortical bone. Since there is a shortage of donors it is imperative that donor bone be used as efficiently as possible.

The Boyce et al '939 reference is a bone derived implant of a composite structure which is made up of at least two superimposed layers of fully mineralized or demineralized or partially demineralized cortical bone material adhesively secured or fastened to each other to form a single rigid structure which was then cut into shaped implants. The implant structure is constructed after demineralization has been undertaken and no amounts of demineralization of the structure have been disclosed. It is not made from a single piece of formed bone. The implant of Boyce et al. '939 is described as noted on Column 5 lines 62-65, "the cortical portion of bone 10 taken from the diaphyseal region is cut into cortical bone layers 11 of varying width by slicing the bone longitudinally". These sections are optionally demineralized. Depending on the thickness of the layers of the composite structure, which are adhesively secured together, can be anywhere from 2 to

200 layers overall, with a thickness ranging from about 0.5 to about 20 mm. A specific overall compression strength for the implant of from about 25 to about 250 Mpa can be obtained. The layers are held together through the use of biological compatible adhesives and mechanical fasteners such as pins, screws, dowels. Figure 2 illustrates an implant comprising alternating layers of fully mineralized cortical bone and partially demineralized cortical bone. Furthermore, there is no discussion of the amount of demineralization and layers are fully mineralized to keep the compression strength of the implant. Example 1 is directed toward slices of mineralized bone and Example 2 is directed toward half of the slices being fully demineralized. As noted in Examples 1 and 2, the slices are held together with cyanoacrylate adhesive. Example 3 is directed to longitudinally cut fully mineralized bars arranged in a lattice structure. In short all that this reference teaches is the assembly of layers of cut cortical bone which are adhesively held together to provide a layered assembly which is then cut into the desired shape. This does not approach or begin to teach the present invention. The Boyce et al. '939 reference teaches away from the present invention.

Furthermore, Boyce et al. '939 does not teach residual calcium left after demineralization because the bone is fully demineralized to achieve osteoinductiveness. The Examiner's response that routine or manipulative experimentation could obtain the ranges of residual calcium are without merit.

The Boyce '187 patent simply teaches an osteoimplant bone composition formed of shaped compressed bone particles. Compressive forces of from about 2,500 to 60,000 psi are applied to bone particles in a mold to produce a hard chalk-like material. There is no teaching using a sheet of cancellous bone as part of a bone sheet in a continuous integral sheet of bone used for surgical repair. Indeed, the prevailing view was that only cortical bone could be used for strength reasons. However, it has been found that cancellous bone can be used and that it has excellent osteoinductive properties.

The reference does not teach or suggest the present invention which has a continuous sheet of demineralized bone with a cortical and cancellous layer.

The court in *Minnesota Mining & Manufacturing Co. v. Johnson &Johnson Orthopaedics, Inc.*, 24 USPQ2d 1321 (Fed. Cir 1992) held that: "Although [a patent's] specific claims are subsumed in [a prior art reference's] generalized disclosure..., this is not literal identity." The *Minnesota* court held that the reference's ranges were so broad as to be meaningless, and provided no guidance on how to construct a product with the patented invention's benefits. The court in *In re Baird,* 29 USPQ2d 1550 (Fed. Cir. 1994) held that "The fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious." The *Baird* court further held that a disclosure to numerous compounds does not render obvious a claim to three compounds, particularly when that disclosure indicates a preference leading away from the claimed compounds.

Applicants would thus submit that the cited references singularly or in combination do not teach or obviate the present invention and that the application should be allowed and be passed to issue.

The Examiner's rejection of the present invention as double patenting in view of claims 1 and 4 of U.S. Patent Number 6,326,018 B1 is without merit as the '018 patent is directed toward a totally different invention. The '018 patent is comprised of demineralized bone particles and a carrier which is lyophilized to remove the water component leaving a flexible static sheet of bone particles. Claims 4 is the addition of a calcium salt which has nothing to do with residual calcium which is left by not completely demineralizing the bone.

An extension of time for three months together with a check for payment of same is attached to this amendment. If any additional costs are incurred, please charge Deposit Account Number 07-

1340.

It is respectfully requested that the arguments and amendments present in the present application in condition for favorable reexamination and that the application be passed to issue.

Respectfully submitted,

GIPPLE & HALE

John S. Hale
Registration No. 25,209

6665-A Old Dominion Drive
McLean, Virginia 22101
(703) 448-1770 ext. 304
Attorney Reference: X-9338

VERSION OF CLAIMS WITH MARKINGS TO SHOW CHANGES MADE

1. A sterile flexible bone sheet for use during the in vivo replacement or reformation of preselected portions of an animal skeletal system comprising a continuous integral unitary sheet of demineralized natural bone [including] with a cortical layer and a cancellous layer [with], the thickness of said sheet ranging from 2.0mm to [about] 8.0mm, the sheet being capable of being bent from its original shape to conform to the configuration of a skeletal region to be repaired without damage to the sheet, said sheet being capable of inducing osteogenesis at the skeletal region.

2. A sterile flexible bone sheet according to claim 1 wherein the thickness of said sheet ranges from [about] 2.0mm to [about] 6.0mm.

3. A sterile flexible bone sheet according to claim 1 wherein the thickness of said cortical layer ranges from [about] 1mm to [about] 4mm and the thickness of said cancellous layer ranges from [about] 1mm to [about] 4mm.

4. A sterile flexible bone sheet according to claim 1 wherein said sheet [includes] has from [about] 1% to [about] 5% hyaluronic acid by weight.

7. A sterile flexible bone sheet according to claim 1 wherein said demineralized sheet has [a] residual calcium [weight] ranging from [about] 3.0% to [about] 8.0% by weight of the demineralized bone mass.

15. A sterile flexible bone sheet for use during the in vivo replacement or reformation of preselected portions of a human bone comprising a continuous unitary sheet of demineralized natural bone including a cortical portion and a cancellous portion with the thickness of said bone sheet ranging from 2.0mm to [about] 6.0mm, said sheet [including] having hyaluronic acid or derivatives thereof with a molecular weight over 700,000 Daltons added thereto at a concentration of 1.0 to 4.0

mg/ml [therein in the range of 1% to 5% by weight], said sheet being flexible for application to a bone to be repaired without damage to the sheet, said sheet being capable of inducing osteogenesis at the bone region.

16. A sterile flexible bone sheet according to claim 15 wherein the thickness of said cortical portion ranges from [about] 1mm to [about] 3mm and the thickness of said cancellous portion ranges from [about] 1mm to [about] 3mm.

17. A sterile flexible bone sheet according to claim 15 wherein said demineralized sheet has [a] residual calcium [weight] ranging from [about] 3.0% to [about] 8.0% by weight of the demineralized bone mass.

20. A sterile flexible bone sheet according to claim 15 wherein said demineralized bone sheet comprises from 99% to 95% by weight of the demineralized cortical cancellous bone [and from 1% to 5% by weight hyaluronic acid].

27. A sterile flexible bone sheet for use during the in vivo replacement or reformation of preselected portions of a human bone comprising a continuous unitary sheet of demineralized natural bone [including] with a cortical layer and a cancellous layer with a cortical/cancellous interface [with], the thickness of said sheet comprising a cortical layer ranging in thickness from [about] 1mm to [about] 3mm and a cancellous layer ranging in thickness from [about] 1mm to [about] 3mm, the sheet being capable of being bent from its original shape to conform to the configuration of a bone to be repaired without damage to the sheet, said sheet being capable of inducing osteogenesis at the [skeletal] bone region.

32. A sterile flexible bone sheet for use during the in vivo replacement or reformation of preselected portions of an animal skeletal system comprising of a continuous unitary sheet of

demineralized natural bone [including] with a cortical layer and a cancellous layer with a cortical cancellous interface, said demineralized bone having a residual calcium weight ranging from [about] 3.0% to 8.0% by weight of the demineralized bone mass with the thickness of said sheet ranging from 2.0mm to 8.0mm, said sheet containing buffered hyaluronic acid or a derivative of same with a molecular weight over 700,000 Daltons [in a range of about 1% to about 5% weight] and having a neutral pH, the bone sheet being capable of being bent from its original shape to conform to the configuration of bone to be repaired without damage to the sheet, said sheet being capable of inducing osteogenesis at the bone region.

33. A sterile flexible bone sheet for use during the in vivo replacement or reformation of preselected portions of a human bone comprising a continuous unitary sheet of demineralized natural bone [including] with a cortical layer, a cancellous layer and a cortical cancellous interface said demineralized natural bone having a residual calcium [weight] ranging from [about] 3.0% to 8.0% by weight of the demineralized bone mass with the thickness of said sheet ranging from [about] 2.0mm to [about] 6.0mm, said sheet containing therein, a hydrogel taken from a group consisting of hyaluronic acid, sodium hyaluronate or derivatives thereof with a molecular weight over 700,000 Daltons [in a range of about 1% to about 5% weight contained therein] and having a neutral pH with an osmolality of [about] 290mmol/kg to [about] 300mmol/kg, the sheet being capable of being bent from its original shape to conform to the configuration of a bone to be repaired without damage to the sheet, said sheet being capable of inducing osteogenesis at said bone to be repaired.

35. A sterile flexible bone sheet according to claim 34 including the step of adding [about] 1% to [about] 5% hyaluronic acid by weight to the bone sheet.

36. A sterile flexible bone sheet according to claim 34 wherein said sheet is demineralized

to have [a] residual calcium [weight] ranging from [about] 3.0% to [about] 8.0% by weight of the demineralized bone mass.